REMARKS

Claims 1-7, 9-11 and 19-27 are in this application.

According to the examiner, claims 19-26 are rejected under 35 USC 112, first paragraph as failing to comply with the enablement requirement. This is respectfully traversed.

The examiner seems to base the rejection on what the Mabalirajan, et al. Journal of Immunology, 183:2059-2067 (2009) article does not disclose. This is not a basis for making a rejection. The scientific literature is replete with articles that describe very narrow fields of research. Many scientists report on the research that they conducted and do not comment on areas outside this research. As explained in column 1 on page 2060, the authors "hypothesized that ESC could have a role in restoring mitochondrial dysfunction and thus is may alleviate asthma features. To determine this, ESC was administered to asthmatic mice and its effects on key mitochondrial structural changes and functions were determined." There is no indication that the authors research extended beyond this and there is no reason to include information on chronic renal disorder, cardio-cerebrovascular disease, etc. that are outside of their scope of research. In addition, as set out in the Information for Authors from the website of the The Journal of Immunology, the articles that are included in the journal are peer-reviewed.

The examiner seems to consider that the description only discloses the effect of the compounds against TGF-β_1 or AngII receptor converting enzyme, but it should be hard to predict from TGF-β_1 or AngII receptor converting enzyme to various diseases, based on a paper published in 2009, whereas, the present invention was completed nearly 7 years ago (counting from the priority date Dec. 5, 2002 of the application).

As mentioned above, reliance on the Mabalirajan article is improper. The TGF-β_1 or AngII receptor converting enzyme have been recognized by the researchers for years, and the relationship between these cell factors/enzymes vs. diseases are quite clear by an ordinary skilled in the art. For instance:

a) Hasegawa et al. US 6,313,153 B1 Nov. 6, 2001,
Title: Compositions and methods for treating nephritis and inhibiting TGF-β_1 related conditions using pyridylacrylamide derivatives

In this patent, it disclosed that, diseases associated with TGF-β_1 may include liver cirrhosis, pulmonary or other fibrosis, nephritis, chronic renal insufficiency, diabetic nephropathy and retinopathy, it is expected that any substances inhibiting TGF-β_1 would be effective aforementioned diseases. A TGF-β_1 inhibiting agent (pyridyl- acrylamide derivative) is a treating agent for liver cirrhosis, pulmonary or other fibrosis, nephritis, chronic renal insufficiency, diabetic nephropathy.

b) Susic, Dinko. *Expert Opin. Invest. Drugs, 9(11), 2593-2600 (English) 2000*
Title: Renal –protective potential of antihypertensive drugs.

In this research paper, it is disclosed that in addition to renoprotection offered by reducing arterial pressure, some antihypertensive agents may give more nephroprotection. Studies indicate that angiotensin-converting-enzyme inhibitors may be more effective in preventing or retarding renal failure than other conventional drugs.

c) Ovid: Park: *Diabetes*, Volume 46(3). March 1997.473-480
Title: Expression of Transforming Growth Factor-beta and Type IV Collagen in Early Streptozotocin-Induced Diabetes

In this research paper, it is disclosed that, insulin treatment substantially inhibited the increased expression of TGF-beta and collagen type IV mRNAs and proteins, TGF-beta is increased in glomeruli during the early phase of rapid renal growth in diabetes, which suggests that TGF-beta may be a key factor involved in the pathogenesis.

as well as:

d) Weir, Matthew R. *Am. J. Hypertens.*, 12(12,Pt.3), 195s-203s, 1999
Title: Are drugs that black the rennin-angiotensin system effective and safe in patients with renal insufficiency?

e) M. E. Marshall, et.al. *J. Cancer Res Clin Oncol* (1994) 120(Sippl): S3-S10
Title: Growth-inhibitory effects of coumarin (1,2-benzopyrone) and 7-hydroxycoumarin on human malignant cell lines in vitro

and

f) R.D. Thornes, et. al. *J. Cancer Res Clin Oncol* (1994) 120(Sippl):s 32- s34
Title: Prevent with coumarin to prevent or delay recurrence of malignant melanoma, etc.

From the references above, it is clear that the relationship between the effects on TGF-β_1 or AngII receptor converting enzyme vs. the indications are familiar to those skilled in the art. In this regard, since in the present invention, the effects on TGF-β_1 or AngII receptor converting enzyme are disclosed, and the relationship between TGF-β_1 or AngII receptor converting enzyme and the diseases are established, there is no undue experimentation.

In addition, the examiner's attention is drawn to examples 3 and 4. In example 3 the data shows that a compound of the invention attenuated glomerular sclerosis and interstitial fibrosis. The examiner's attention

As claims 19-26 are enabled, it is respectfully requested the rejection be withdrawn.

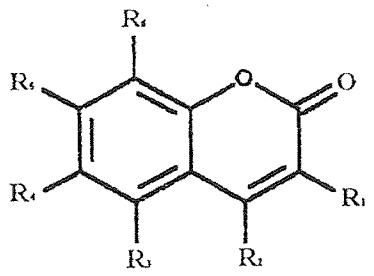
The Examiner has rejected claims 1-2, 4, 6-7 and 9-11 under 35 USC 102(b) as being anticipated by Chinese Patent number , CN12307392. This is respectfully traversed.

Anticipation requires that each and every element of the claimed invention be disclosed in a single prior art reference. In re Paulsen, 30 F.3d 1475, 31 USPQ 1671 (Fed. Cir. 1994). For anticipation, there must be no difference between the claimed invention and the reference disclosure, as viewed by a person of ordinary skill in the field of the invention. Scripps Clinic & Res. Found. v. Genentech, Inc., 927 F.2d 1565, 18 USPQ2d 1001 (Fed. Cir. 1991).

CN12307392 claims a compound of the formula I, which is a retinoyl coumarine derivative, and the compounds disclosed therein all comprise retinoyl groups, thus CN12307392 is irrelevant with the present invention.

Specifically, the claim 1 of CN12307392 reads:

> 1. A **retinoylcoumarin** compound as represented by the following formula I and the pharmaceutically acceptable salt thereof:



(I)

wherein, R_1 is H, C_1- C_{18}-alkyl, aralkyl and haloalkyl, $CXYR^7$, wherein X is H, N, NH, C, CH, O, and Y is H, N, NH, C, CH, O, and XY is O, R^7 is H, halogen, OH, C_1- C_{18}-alkyl, haloalkyl, alkoxyl, ester group, unsubstituted, mono- or multi substituted phenyl, wherein the substituent on the benzene ring can be C_1- C_4-alkyl, haloalkyl, alkoxyl, OH, halogen, CO_2H, ester group, NO_2, CF_3, SO_3H, NR^8R^9, wherein R^8 and R^9 are same and different, respectively independently being H, alkyl, cycloalkyl and in combination form a heterocycle, etc;

R^2 is H, C_1- C_{18}-alkyl, haloalkyl, alkoxyl, ester group, halogen, OH, phenyl or substituted phenyl, $CXYR^7$, OR wherein X, Y and R^7 are as defined above, R = retinoyl;

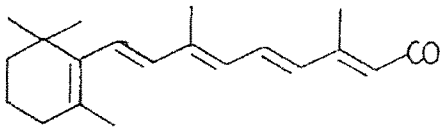
R^3 is H, OH, CHC_2OH, halogen, C_1- C_{18}-alkyl, haloalkyl, ester group, alkoxyl, OR, CH_2OR or $CXYR^7$, wherein R, X, Y and R^7 are as defined above;

R^4 is H, halogen, C_1- C_{18}-alkyl, haloalkyl, alkoxyl, ester group, OH, $CXYR^7$, wherein X, Y and R^7 are as defined above;

R^5 is H, C_1- C_{18}-alkyl, haloalkyl, alkoxyl, halogen, ester group, OR or $CXYR^7$, wherein R^7, X, Y and R are as defined above;

R^6 is H, C_1- C_{18}-alkyl, haloalkyl, alkoxyl, halogen, ester group, OH, OR, $CXYR^7$, wherein R, X, Y and R^7 are as defined above;

From the description of CN12307392, Retinoyl means:



Thus, since the subject of the compounds of CN12307392 is retinoylcoumarin, there must be retinoyl group in the compound structure. In contrast with this, the compounds as claimed in claim 1 of present application where R_3 may be $CONHR_9$, and R_9 may be phenyl either unsubstituted or substituted with hydroxyl, alkoxyl, carboxyl, NO_2, halogen or SO_3H, and R_4-R_8 are all hydrogen is not within the

compounds of CN12307392, thus the present invention is not anticipated by CN12307392.

Therefore, it is respectfully requested that the rejection be withdrawn.

It is submitted that the present application is in condition for allowance.

Respectfully submitted,

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